Identifying Vasopressor and Inotrope Use for Health Services Research

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Abstract

Rationale: Identifying vasopressor and inotrope (vasopressor) use from administrative claims data may provide an important resource to study the epidemiology of shock.

Objectives: Determine accuracy of identifying vasopressor use using International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) coding.

Methods: Using administrative data enriched with pharmacy billing files (Premier, Inc., Charlotte, NC), we identified two cohorts: adult patients admitted with a diagnosis of sepsis from 2010 to 2013 or pulmonary embolism (PE) from 2008 to 2011. Vasopressor administration was obtained using pharmacy billing files (dopamine, dobutamine, epinephrine, milrinone, norepinephrine, phenylephrine, vasopressin) and compared with ICD-9-CM procedure code for vasopressor administration (00.17). We estimated performance characteristics of the ICD-9-CM code and compared patients' characteristics and mortality rates according to vasopressor identification method.

Measurements and Main Results: Using either pharmacy data or the ICD-9-CM procedure code, 29% of 541,144 patients in the sepsis cohort and 5% of 81,588 patients in the PE cohort were identified as receiving a vasopressor. In the sepsis cohort, the ICD-9-CM procedure code had low sensitivity (9.4%; 95% confidence interval, 9.2–9.5), which increased over time. Results were similar in the PE cohort (sensitivity, 5.8%; 95% confidence interval, 5.1–6.6). The ICD-9-CM code exhibited high specificity in the sepsis (99.8%) and PE (100%) cohorts. However, patients identified as receiving vasopressors by ICD-9-CM code had significantly higher unadjusted in-hospital mortality, had more acute organ failures, and were more likely hospitalized in the Northeast and West.

Conclusions: The ICD-9-CM procedure code for vasopressor administration has low sensitivity and selects for higher severity of illness in studies of shock. Temporal changes in sensitivity would likely make longitudinal shock surveillance using ICD-9-CM inaccurate.

Keywords: vasoconstrictor agents; shock; international classification of diseases; sepsis; pulmonary embolism

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Shock is a state of tissue hypoperfusion that may lead to organ dysfunction and death, affecting approximately one of three patients hospitalized in an intensive care unit (1). Vasopressor and inotropic medications (herein referred to as “vasopressor medications”) act to reverse the cardiovascular and hemodynamic

collapse associated with shock to restore tissue perfusion (2). The ability to accurately identify vasopressor medication use from standard administrative claims data may provide an important resource to study the clinical epidemiology of shock. Several studies (3–7) have sought to use the vasopressor International Classification

of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) code from standard administrative data to investigate the administration of vasopressor medications; however, the validity of using the ICD-9-CM procedure code for vasopressor administration has not been explored. The accuracy of ICD-9-CM

diagnosis and procedure codes has been found to vary widely, often depending on reimbursement rates associated with specific codes (8–11). For example, major procedures performed in operating rooms have been found to be more accurately recorded than minor bedside procedures (12).

We sought to explore ICD-9-CM vasopressor procedure code accuracy among patients with sepsis or pulmonary embolism, two common conditions that lead to hospitalization and may result in shock requiring use of vasopressor medications. We sought to leverage a large sample of hospitalizations in the United States from an enhanced administrative dataset enriched with detailed pharmacy billing files to evaluate the accuracy and potential for misclassification associated with vasopressor medication use identified from ICD-9-CM procedure codes in standard claims data.

Methods

We identified two cohorts using the Premier (Premier, Inc., Charlotte, NC) enhanced administrative database, which includes date-stamped pharmacy and diagnostics billing information from more than 500 hospitals in the United States representing approximately 20% of U.S. hospitalizations. For the primary analysis, we identified adult patients admitted with a diagnosis of sepsis or septic shock (ICD-9-CM codes 0.38x, 995.91, 995.92, 785.52) between 2010 and 2013. This algorithm to select the sepsis cohort was chosen to maximize specificity and positive predictive value (PPV) while maintaining moderate sensitivity (13, 14). To explore variation in accuracy of vasopressor codes across diagnoses, we also investigated a secondary cohort of adult patients hospitalized with

pulmonary embolism (PE; ICD-9-CM codes 415.1, 415.11, 415.12, 415.13, 415.19, 673.2) between 2008 and 2011. For each cohort we identified vasopressor medication administration during the hospitalization using (1) pharmacy billing files as the gold standard (dopamine, dobutamine, epinephrine, milrinone, norepinephrine, phenylephrine, vasopressin), and (2) the ICD-9-CM procedure code for vasopressor administration (00.17). Pharmacy billing files include details regarding drug, dose, formulation, day, and route of administration; Premier, Inc. regularly audits data collection at source hospitals to ensure quality and integrity and performs additional data validation after receipt from participating hospitals. We also extracted patient demographics, comorbid conditions, and acute organ failures present on admission as well as hospital characteristics and information related to the patient's hospitalization (location of care, attending physician of record, primary payer).

Statistical Analysis

We estimated the performance characteristics of the ICD-9-CM procedure code for vasopressors by calculating sensitivity, specificity, PPV, and negative predictive value (NPV). Furthermore, we characterized temporal trends in code validity over time using the Cochrane-Armitage test of trend.

We performed two sensitivity analyses to test the robustness of our findings. First, we analyzed the subgroup of patients with sepsis and a surgeon as attending physician of record to explore generalizability of the results to a surgical population. Second, we excluded patients who received mechanical ventilation and phenylephrine for fewer than two consecutive days to test for potential

misclassification of patients who received vasopressor medications transiently during endotracheal intubation.

To evaluate the potential for misclassification of vasopressor medication exposure to induce bias, we compared differences in baseline characteristics and hospital mortality rates between patients who had an ICD-9-CM procedure code for vasopressor administration and patients identified as receiving vasopressor medications through pharmacy billing files. We used standardized differences with a threshold of 0.1 (15), because in cohorts with a large sample size the Chi-square test may show clinically insignificant between-group statistical differences (16). We used SAS version 9.4 (Cary, NC) for all analyses. Study procedures were approved by the Boston University Medical Campus Institutional Review Board.

Results

Among 541,144 patients in the sepsis cohort, 142,406 (26.3%) were identified as receiving a vasopressor medication by pharmacy data alone, 911 (0.2%) by ICD-9-CM code alone, and 14,701 (2.7%) by both. Among 81,588 patients in the PE cohort, 3,759 (4.6%) were identified as receiving a vasopressor medication by pharmacy data alone, 37 (0.03%) by ICD-9-CM code alone, and 233 (0.3%) by both. When compared with pharmacy billing files, the vasopressor ICD-9-CM procedure code had a sensitivity of 9.4% (95% confidence interval [CI], 9.2–9.5), specificity of 99.8% (95% CI, 99.8–99.8), PPV of 94.1% (95% CI, 93.8–94.5), and NPV of 72.9% (95% CI, 72.8–73) in the sepsis cohort and sensitivity of 5.8% (95% CI, 5.1–6.6), specificity of 100% (95% CI, 99.6–100), PPV of 89.6% (95% CI, 85.3–93), and NPV of 95.4% (95% CI, 95.2–95.5) in the PE cohort.

Table 1. Performance characteristics of the International Classification of Disease, Ninth Revision, Clinical Modification vasopressor code in a subgroup of surgical patients and a subsample excluding patients who may have received transient phenylephrine during intubation

Sensitivity Analysis	N	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Surgical patients, sepsis cohort	24,184	8.9 (8.4–9.4)	99.7 (99.6–99.8)	96 (94.8–97.2)	58.6 (57.9–59.2)
Excluding transient phenylephrine, sepsis cohort	622,732	8.5 (7.9–9.1)	99.7 (99.6–99.8)	94.8 (93.2–96.4)	64 (63.3–64.6)
Excluding transient phenylephrine, PE cohort	622,732	6.9 (3.3–10.5)	99.9 (99.8–100)	92.9 (79.4–100)	88.7 (87.1–90.3)

Definition of abbreviations: NPV = negative predictive value; PE = pulmonary embolism; PPV = positive predictive value.

Table 2. Baseline characteristics of the sepsis and pulmonary embolism cohorts stratified by method of identification of vasopressor medication use

Variable	Sepsis Cohort			Pulmonary Embolism Cohort		
	ICD-9-CM Code (N = 15,612)	Pharmacy Only (N = 142,406)	Standardized Difference*	ICD-9-CM Code (N = 260)	Pharmacy Only (N = 3,759)	Standardized Difference*
Hospital mortality	5,810 (37.2)	43,257 (30.4)	0.15	126 (48.5)	1,306 (34.7)	0.28
Age, mean (SD), yr	66.9 (15.2)	66.7 (15.5)	0.01	67.1 (15.7)	66 (14.9)	0.08
<55	3,153 (20.2)	29,658 (20.8)		52 (20)	840 (22.4)	
55–74	6,937 (44.4)	62,295 (43.7)		108 (41.5)	1,705 (45.4)	
75+	5,522 (35.4)	50,453 (35.4)		100 (38.5)	1,214 (32.3)	
Sex, female	7,952 (50.9)	70,309 (49.4)	0.03	143 (55)	2,048 (54.5)	0.01
Race			0.09			0.08
White	10,949 (70.1)	96,797 (68)		172 (66.2)	2,462 (65.5)	
Black	1,687 (10.8)	18,600 (13.1)		43 (16.5)	609 (16.2)	
Hispanic	137 (0.9)	2,122 (1.5)		12 (4.6)	135 (3.6)	
Other/unknown	2,839 (18.2)	24,887 (17.5)		33 (12.7)	553 (14.7)	
Geographic location			0.36			0.38
Northeast	3,937 (25.2)	20,120 (14.1)		58 (22.3)	499 (13.3)	
Midwest	1,766 (11.3)	27,194 (19.1)		63 (24.2)	829 (22.1)	
South	6,075 (38.9)	67,071 (47.1)		79 (30.4)	1,773 (47.2)	
West	3,834 (24.6)	28,021 (19.7)		60 (23.1)	658 (17.5)	
Teaching hospital status	6,729 (43.1)	55,893 (39.3)	0.08	97 (37.3)	1,482 (39.4)	0.04
Specialty of attending physician			0.02			0.12
Pulmonary/CCM	1,770 (11.3)	15,900 (11.2)		41 (15.8)	489 (13)	
Cardiology	273 (1.8)	2,518 (1.8)		21 (8.1)	246 (6.5)	
Other medical specialty	12,576 (80.6)	114,262 (80.2)		184 (70.8)	2,845 (75.7)	
Surgery	978 (6.3)	9,616 (6.8)		14 (5.4)	175 (4.7)	
Non-healthcare facility point of origin	11,376 (72.9)	107,316 (75.4)	0.06	91 (35)	1,159 (30.8)	0.09
Length of stay, mean (SD)	11.8 (13.6)	12 (14.3)	0.02	9.1 (9.5)	10.4 (10.8)	0.13
Primary payor			0.06			0.09
Medicare	10,518 (67.4)	94,939 (66.7)		156 (60)	2,323 (61.8)	
Medicaid	1,432 (9.2)	15,361 (10.8)		18 (6.9)	311 (8.3)	
Private Insurance	2,523 (16.2)	22,386 (15.7)		69 (26.5)	870 (23.1)	
Self-pay	642 (4.1)	5,577 (3.9)		8 (3.1)	137 (3.6)	
Other	497 (3.2)	4,143 (2.9)		9 (3.5)	118 (3.1)	
Prevalent comorbidity, mean (SD)	2.6 (1.6)	2.5 (1.6)	0.04	1.4 (1.1)	1.4 (1.1)	0.02
Diabetes mellitus	5,402 (34.6)	51,927 (36.5)	0.04	66 (25.4)	986 (26.2)	0.02
Hypertension	9,427 (60.4)	86,541 (60.8)	0.008	154 (59.2)	2,134 (56.8)	0.05
Heart failure	5,224 (33.5)	44,133 (31)	0.05	33 (12.7)	381 (10.1)	0.08
Stroke or TIA	278 (1.8)	2,498 (1.8)	0.002	†	†	
Atrial fibrillation	3,777 (24.2)	33,309 (23.4)	0.02	48 (18.5)	610 (16.2)	0.06
Ischemic heart disease	4,409 (28.2)	39,223 (27.5)	0.02	0 (0)	15 (0.4)	0.09
Chronic pulmonary disease	5,478 (35.1)	47,162 (33.1)	0.04	17 (6.5)	236 (6.3)	0.01
Peripheral vascular disease	1,865 (12)	17,174 (12.1)	0.004	10 (3.9)	159 (4.2)	0.02
Cancer	2,326 (14.9)	19,124 (13.4)	0.04	28 (10.8)	541 (14.4)	0.11
Dementia	626 (4)	6,107 (4.3)	0.01	5 (1.9)	179 (4.8)	0.16
Number of acute organ failures, mean (SD)	2 (1.2)	1.8 (1.2)	0.19	1 (1.2)	0.7 (1)	0.26
Respiratory	7,840 (50.2)	63,295 (44.5)	0.12	101 (38.9)	999 (26.6)	0.26
Renal	10,640 (68.2)	91,522 (64.3)	0.08	52 (20)	715 (19)	0.02
Neurologic	2,914 (18.7)	22,739 (16)	0.07	31 (11.9)	263 (7)	0.17
Hematologic	3,122 (20)	27,412 (19.3)	0.02	26 (10)	313 (8.3)	0.06
Metabolic	6,086 (39)	43,842 (30.8)	0.17	43 (16.5)	374 (10)	0.2
Hepatic	1,386 (8.9)	10,022 (7)	0.07	13 (5)	107 (2.9)	0.11
Year of hospitalization			0.09			0.19
2008	—	—		51 (19.6)	981 (26.1)	
2009	—	—		81 (31.2)	1,108 (29.5)	
2010	2,150 (13.8)	22,641 (15.9)		70 (26.9)	1,039 (27.6)	
2011	4,969 (31.8)	48,337 (33.9)		58 (22.3)	631 (16.8)	
2012	5,728 (36.7)	48,101 (33.8)		—	—	
2013	2,765 (17.7)	23,327 (16.4)		—	—	

Definition of abbreviations: CCM = critical care medicine; ICD-9-CM = International Classification of Disease, Ninth Revision, Clinical Modification; TIA = transient ischemic attack.

Data presented as n (%) unless otherwise noted.

*Boldface type demonstrates absolute standardized difference ≥ 0.1 , which denotes a clinically significant difference between groups.

†N < 5 within group.

Performance characteristics of the vasopressor ICD-9-CM code were similar in a surgical subgroup of septic patients and a subsample that excludes patients who may have received phenylephrine transiently during intubation (Table 1).

Baseline characteristics for patients with sepsis and PE stratified by method of identification of vasopressor medication are shown in Table 2. Compared with patients who were identified as having received a vasopressor medication solely through the pharmacy billing file, patients who had an ICD-9-CM procedure code for vasopressor use had significantly higher unadjusted in-hospital mortality, were more likely to be hospitalized in the Northeast and West, and had more acute organ failures. Comorbid conditions were generally balanced between both groups in the cohorts. In both the sepsis and PE cohorts we identified a significant temporal trend toward increased use and sensitivity (Cochran-Armitage Trend Test $P < 0.0001$ and 0.01 , respectively) of the vasopressor ICD-9-CM procedure code over time (Figure 1).

Discussion

We characterized the validity of ascertaining vasopressor medication use with the ICD-9-CM procedure code for vasopressor administration, as compared with pharmacy billing files, among patients hospitalized with sepsis or PE from a large enhanced administrative database of hospitalizations in the United States. The ICD-9-CM procedure code showed poor sensitivity

(<10%) when compared with detailed pharmacy billing data, a situation that would lead to significant misclassification of vasopressor medication exposure in conventional administrative data that do not include pharmacy billing files. In the sepsis cohort, which was chosen using an ICD-9-CM algorithm with moderate sensitivity and high specificity compared with chart-abstracted data (13, 14), the true sensitivity of using the ICD-9-CM vasopressor code to identify vasopressor medication use would be even lower. Furthermore, changes in sensitivity of vasopressor ICD-9-CM codes over time limit the utility of using ICD-9-CM vasopressor codes to study epidemiological trends in vasopressor medication use. The similarity in performance for cases of shock due to sepsis and pulmonary embolism suggests that these findings are robust across diverse disease entities, and results from a surgical subgroup suggest robustness across treating specialties.

Our findings are consistent with a prior study showing that ICD-9-CM procedure codes had poor sensitivity and reliability compared with chart review for minor procedures, such as those performed on wards or in radiology departments (12). In a recent study, intravenous tissue plasminogen activator administration was found to be undercoded by 20% when comparing ICD-9-CM procedure code to a confirmed stroke registry (17).

We characterized the potential for selection bias associated with use of the ICD-9-CM procedure code to ascertain patients who received a vasopressor medication. Studies using the vasopressor

ICD-9-CM code would oversample patients from the Northeastern and Western states, as well as patients with greater illness severity, who have more acute organ failures and higher mortality rates than the underlying population of patients receiving vasopressor medications identified through pharmacy files.

We demonstrate that differences in characteristics are robust for sepsis and pulmonary embolism, two common conditions with different prevalence of shock requiring administration of vasopressor medications.

A recent study using the Danish National Patient Registry reported high PPV of the ICD-10 procedure code for vasopressor administration in identifying presence of shock when used alone and in combination with shock ICD-10 diagnosis codes (18). Our study demonstrated a similarly high PPV of the ICD-9-CM procedure code for the proximate event of vasopressor medication administration in a U.S. population. The high specificity and PPV associated with the vasopressor ICD-9-CM procedure code would allow investigators to identify a highly selected sample of patients with vasopressor medication-dependent shock. Such a strategy may be helpful when avoiding false-positive cases of shock is paramount; however, a sample selected with the ICD-9-CM procedure code would have higher illness severity and would not be representative of the underlying population of patients with shock. As a consequence, results from such studies may have limited generalizability. Furthermore, poor sensitivity would mean that absence of a vasopressor ICD-9-CM code would not reliably rule out the absence of shock requiring vasopressor medications.

Our study had limitations that should be considered when interpreting the findings. First, we were unable to definitively rule out vasopressor medication use for indications other than shock; however, a sensitivity analysis excluding patients who may have received transient phenylephrine injection during intubation showed similar results to the primary analysis. Furthermore, the Premier dataset overrepresents smaller hospitals and those in the Southern United States, potentially limiting generalizability. Finally, pharmacy billing files potentially identify vasopressor medications that were never administered to the patient, although standard billing

Figure 1. Trend over time of sensitivity of identifying patients receiving a vasopressor medication through the International Classification of Disease, Ninth Revision, Clinical Modification vasopressor procedure code versus pharmacy billing files. PE = pulmonary embolism.

practice is to charge for a medication on administration.

Using a large sample of patients hospitalized with sepsis or PE across the United States, we demonstrated that the ICD-9-CM procedure code for vasopressor administration had very low sensitivity but high PPV for identifying patients who had a vasopressor medication administered during hospitalization when

compared with pharmacy billing data. Use of the vasopressor ICD-9-CM procedure code to ascertain patients who received a vasopressor medication would likely result in a small subsample of patients with greater severity of illness and in-hospital mortality than patients identified with pharmacy charge data, introducing bias through misclassification of patients, which may lead to erroneous conclusions

about severity of illness, treatment administration, and outcomes. Furthermore, use of the ICD-9-CM vasopressor code to identify temporal trends in shock may introduce variable systematic error that would make temporal comparisons inaccurate. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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